Complete Summary

GUIDELINE TITLE

Rectal cancer.

BIBLIOGRAPHIC SOURCE(S)

National Working Group on Gastrointestinal Cancers. Rectal cancer. Amsterdam, The Netherlands: Association of Comprehensive Cancer Centres (ACCC); 2008 Oct 14. 82 p. [306 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Rectal cancer (adenocarcinomas only)

GUIDELINE CATEGORY

Counseling
Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Colon and Rectal Surgery
Family Practice

Gastroenterology
Internal Medicine
Nuclear Medicine
Nursing
Oncology
Pathology
Pharmacology
Radiation Oncology
Radiology

INTENDED USERS

Advanced Practice Nurses
Nurses
Pharmacists
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To provide recommendations to aid healthcare professionals involved in the treatment of patients with rectal cancer to aid in daily practice
- To provide a basis for counseling patients
- To provide better treatment and thereby better outcomes for patients
- To provide a starting point for developing transmural arrangements or local protocols to promote implementation

TARGET POPULATION

Adult men and women in the Netherlands with rectal cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Diagnosis
    - Local staging using endorectal ultrasound, magnetic resonance imaging
    - Location of tumors
    - Assessment of pelvic lymph nodes
    - Screening for distant metastases using abdominal computed tomography and chest x-ray
2. Pathology assessment of resected specimen
    - Information on standard pathology report
    - Minimum number of lymph nodes to determine N stage
    - TNM classification
3. Assessment after neoadjuvant therapy
4. Assessment of the circumferential resection margin

Management/Treatment

1. Radiotherapy
    - Preoperative radiotherapy
    - Preoperative versus postoperative combined chemoradiotherapy using capecitabine
    - Postoperative radiotherapy
    - Intraoperative radiotherapy or brachytherapy
2. Surgery
    - Local excision
    - Total mesorectal excision (TME)
    - Transanal excision (TAE)
    - Transanal endoscopic microsurgery (TEM)
3. Laparoscopic surgery (recommended for rectal surgery only in controlled setting with sufficient expertise)
    - Minimum surgeon training requirements
4. Treatment of stage T4 rectal cancer and locally recurrent disease
    - Treatment in specialized centers
    - Neoadjuvant therapy
    - Data registration and reporting
5. Adjuvant chemotherapy (no clear recommendations given)
6. Follow-up up for local recurrence
    - Coordination of care
    - Frequency of follow-up
    - Method of follow-up: colonoscopy, digital rectal examination, hepatic ultrasound or computed tomography (CT) scan, carcinoembryonic antigen (CEA) assessment
7. Treatment of metastases
    - Combination of fluoropyrimidine-containing chemotherapy plus bevacizumab
    - Oral fluoropyrimidines versus 5-fluorouracil/leucovorin
    - Oxaliplatin or irinotecan as a component of first-line combination chemotherapy
    - Hyperthermic intraperitoneal chemotherapy (HIPEC)
8. Communication
    - Use of a multidisciplinary oncology review board
    - Informing patients about their disease and available treatment options
    - Clearly defining the care provider(s) responsible for communication
    - Informing about patient organizations

MAJOR OUTCOMES CONSIDERED

- Sensitivity and specificity of diagnostic studies
- Degree of tumor regression
- Rate of obtaining negative resection margins
- Local recurrence rate
- Overall and disease-free survival rates
- Morbidity
- Rate of conversion from laparoscopic to open surgery
- Complications and adverse effects of therapy
- Duration of hospitalization
- Quality of life
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The recommendations in this guideline are based as much as possible on evidence from published scientific research. The first step was to search for related guidelines recently published outside the Netherlands. If available, these were used as a starting point; systematic literature searches were then performed to identify relevant articles published after the foreign guidelines had been published. Relevant articles were identified by performing systematic searches in the Cochrane Library, Medline, and, if deemed necessary, Embase, Cinahl, and Psychinfo. Languages were limited to English, German, French, and Dutch. Manual searches were also performed. If foreign guidelines were available, searches covered the period starting at the publication date of the foreign guideline and ending in February 2006. If foreign guidelines were not available, searches covered the period from 1980 to February 2006. Some more recent articles were also included. For the search terms used, see appendix 13 in the original guideline document.

Case reports were excluded. Some articles found in the reference lists of obtained articles were also included. At this point, articles were then selected based on inclusion and exclusion criteria. Key inclusion criteria were comparative studies with high level of evidence, such as meta-analyses, systematic reviews, randomised controlled trials (RCTs), and controlled trials (CTs). If these were not available, comparative cohort studies, comparative patient-control studies, and non-comparative studies were considered. Other important criteria included sufficient study size and follow-up, adequate ruling out of selection bias, and results that apply to the situation in the Netherlands.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Classification of Supporting Evidence Based on the Level of Evidence

For Articles Regarding Intervention (Prevention or Therapy)

A1	Systematic reviews covering at least some A2-level studies in which the results of the individual studies are consistent
A2	Randomised comparative clinical studies of good quality (randomised, double blind) and sufficient size and consistency
B	Randomised clinical trials of moderate quality or insufficient size, or other comparative studies (non-randomised, comparative cohort studies, patient-control studies)
C	Non-comparative studies
D	Expert opinion from, for example, working group members
For Articles Regarding Diagnosis	
A1	Studies on the effects of diagnosis on clinical outcomes in a prospectively followed, well defined patient population with a predefined protocol based on the results of the study test, or decision theory studies on the effects of diagnosis on clinical outcomes based on the results of A2-level studies with sufficient consideration given to the interaction between diagnostic tests
A2	Studies that include a reference test with predefined criteria for the study test and the reference test and a good description of the test and the clinical population studied; a sufficiently large series of consecutive patients must be included, predefined cut-off values must be used and the results of the test and the gold standard must be evaluated independently. For situations in which multiple diagnostic tests are involved, there is in principle interaction and the analysis should take this into account by using, for example, logistical regression
B	Comparison with a reference test and description of the study test and population, but lacking the other characteristics of A-level studies
C	Non-comparative studies
D	Expert opinion from, for example, working group members
Level of Evidence for Conclusions	
1	At least 1 systematic review (A1) or 2 independently conducted A1- or A2-level studies
2	At least 2 independently conducted B-level studies
3	At least 1 A2-, B- or C-level study
4	Expert opinion from, for example, working group members

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The quality of the selected articles was evaluated using evidence-based guideline development (evidence-based richtlijnontwikkeling, EBRO) evaluation forms. Articles of mediocre or poor quality were excluded. After this selection process,

the remaining articles were used as the basis for the various conclusions found in the guideline. The selected articles were then graded according to the level of evidence using the classification system described in the section "Rating Scheme for the Strength of the Evidence."

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The National Working Group on Gastrointestinal Cancers (Landelijke Werkgroep Gastro-Intestinale Tumoren) initiated the guideline and formulated a number of clinical questions (see appendix 1 in the original guideline document). These questions address the problems encountered in daily practice regarding the diagnosis, treatment, and follow-up of patients with rectal cancer.

Each clinical question was assigned to no more than one or two members of the working group. Each working group member performed systematic searches with the help of an information specialist from the Dutch Institute for Healthcare Improvement (CBO) to identify literature relevant to his or her clinical question. Selected articles were summarised by CBO epidemiologists under the direction of working group members. Working group members then drafted the scientific conclusions, other considerations, and recommendations. The working group worked on the draft text for the guideline for approximately one year. Texts were discussed during plenary sessions and, after comments were incorporated, agreed upon by all authors. Given that a working group for the rectal cancer guideline was established at the same time as the working group for the colon cancer guideline, it was decided to organise joint plenary sessions to ensure efficiency and good correlation between the two guidelines. An editorial team, consisting of the working group chairs and representatives from the Vereniging voor Integrate Kankercentra (VIKC), were responsible for coordination and reaching consensus among working group members. The complete working group met on six occasions to discuss the results. The individual texts were combined and revised for consistency by the editorial team to create one document: the draft guideline.

In addition to the scientific evidence, there are often other important aspects to consider in the development of a recommendation, including patient preferences, the availability of special techniques or expertise, organisational factors, societal consequences, and costs. These factors are addressed in the section following the 'Conclusion' under the tab 'Considerations'. In this section, the conclusion that was based on the literature is placed in the context of daily practice, and the advantages and disadvantages of the various policy options are weighed. The final formulated recommendation is the result of the available evidence combined with these considerations. The output of this procedure and the structuring of the guideline in this format are intended to enhance the transparency of the guideline. It allows for efficient discussion during the study group meetings and also increases the clarity for guideline users.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Level of Evidence for Conclusions	
1	At least 1 systematic review (A1) or 2 independently conducted A1- or A2-level studies
2	At least 2 independently conducted B-level studies
3	At least 1 A2-, B-, or C-level study
4	Expert opinion from, for example, working group members

COST ANALYSIS

Cost-Effectiveness of Laparoscopic Surgery

In the National Institute for Health and Clinical Excellence (NICE) report, the cost-effectiveness of laparoscopic surgery was compared with that of open surgery based on five primary studies and a self-conducted economic analysis. Compared with open surgery, the average costs for laparoscopic surgery were higher in four of the five studies. However, the reported costs varied greatly and the studies were considered of mediocre quality. Assuming that the long-term costs are similar, it is important to determine whether the short-term advantages of laparoscopic surgery (as a result of faster recovery) compensate for the extra costs. The difference in duration of hospitalisation is one of the most important determinants to consider.

The total costs associated with the laparoscopic technique may be comparable to those of the open technique if sociological advantages are included, such as earlier hospital discharge and faster resumption of employment. Over the long term, the number of re-interventions, particularly for incisional hernia, may also be reduced. Little hard evidence on these issues is available.

Effect of Optimal Follow-up on Costs

Estimates of the cost-effectiveness of intensive follow-up in patients with colorectal carcinoma vary from 1,000 euro per QALY to more than 20,000 euro per QALY.

There is evidence that ultrasound is the most cost-effective follow-up test. Estimates of the cost-effectiveness of carcinoembryonic antigenÂ (CEA) assessment vary widely.

See the original guideline document for a more detailed discussion of the costs related to follow-up.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The draft guideline was presented to relevant scientific organisations and regional Integrate Kankercentra (IKC) working groups for discussion on 12 April 2007. After comments were incorporated, the guideline was endorsed by the complete working group and submitted to the relevant professional societies for authorisation on 10 July 2007.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Diagnosis

All cases of rectal cancer should be discussed in a multidisciplinary oncology review board.

Local staging of rectal cancer has important implications in determining the optimal treatment approach. Endorectal ultrasound has an important role in the staging of superficial tumours. This technique is preferred over magnetic resonance imaging (MRI) to differentiate between T1 and T2 superficial tumours.

For non-superficial tumours, MRI should be considered part of the standard work-up, especially for the accurate assessment of circumferential resection margins, which is particularly important for determining optimal therapy.

Tumours located 5 mm or more from the mesorectal fascia have a low risk of a positive circumferential resection margin.

Pelvic lymph nodes 5 mm or larger in diameter according to MRI should be considered positive.

Patients should be screened for distant metastases using abdominal computed tomography (CT) and chest x-ray (see the guideline 'Colorectal liver metastases' [in Dutch]).

Considerations

It should be noted that the results of the endorectal ultrasound (EUS) studies were influenced to some degree by the fact that selection bias may have occurred: high and stenosing tumours, which are difficult to access with EUS, may have been excluded.

Many of the included studies on EUS were conducted in specialised centres. Based on one study, it appears that EUS results depend on the level of expertise of the centre: better results are achieved in specialised centres than in non-specialised centres. Nationally and internationally, there is a growing trend toward increased use of MRI in local staging, particularly for identifying large tumours. An optimal MRI sequence is important in this setting. In the literature, various definitions are used to determine the risk of invaded circumferential resection margin. Tumours located within 1 mm of the mesorectal fascia are considered 'involved', and tumours located 2-5 mm from the fascia are considered 'close'. Tumours located 5

mm or more from the facia are considered to have a low risk of invaded circumferential resection margin (CRM).

Lymph nodes pose a different problem. At this time, there is no reliable method for determining lymph node status prior to surgery. It is known that the risk of tumour involvement in nodes >10 mm is 93%. For smaller nodes, this becomes more problematic: the risk of tumour involvement in lymph node 2-5 mm in diameter on MRI is 50%. The risk is higher for nodes larger than 5 mm. Therefore, the working group is of the opinion that lymph nodes larger than 5 mm on MRI must be considered positive.

It is also the opinion of the experts that patient care benefits from MRI interpretation by the radiologist as well as by the surgeon and the radiotherapist. The ideal forum for this is a multidisciplinary oncology review board.

Pathology

Standard Pathology Report

The pathology report should include at least the following information:

- Histological tumour type
- Histological tumour grade
- Extent of invasion (T stage)
- Distance between the tumour and the nearest resection margin, and the completeness of resection
- Number of excised and affected lymph nodes (N stage)
- Tumour size
- Circumferential margin (positive, negative, distance in mm)
- Quality of surgery (see the section "CRM and the Quality of Surgery" in the original guideline document)

The following information is optional:

- Perineural invasion
- Macroscopic description of the tumour
- Vascular invasion
- Lymphatic invasion

The standard report is preferred. Requirements differ for resected specimens from patients who have undergone neoadjuvant therapy (see the section "Assessment after neoadjuvant chemotherapy" in the original guideline document).

For definitions of terms used in the pathology report, see appendix 12 in the original guideline document.

Minimum Number of Lymph Nodes

Determining the lymph node status of a patient requires evaluating as many lymph nodes as possible using conventional techniques (haematoxylin and eosin

[HE] without pre-treatment). A minimum of 10 lymph nodes is recommended to establish a negative lymph node status.

Considerations

No definitive criteria were found in the literature regarding the minimum number of lymph nodes to be evaluated. There is no evidence to support 12 lymph nodes, as recommended by TNM. Current staging for colorectal cancer is based on HE assessment without special pretreatment. Therefore, immunohistochemical staining to detect metastases or pretreatment with acetic acid or similar agents is not recommended.

Evaluation of less than 10 lymph nodes is increasingly used to define patients with high-risk TNM stage II disease. It therefore seems reasonable to maintain a minimum requirement of 10 lymph nodes.

TNM

Preferred Version of TNM Classification

At this time, use of the TNM 5 (1997) classification should be used. It should be noted that it is reasonable to report the presence or absence of tumour deposits and their characteristics separately.

Prognostic Histopathological Factors in TNM Stage II Disease

To identify patients with high-risk TNM stage II disease, the working group recommends adhering to the American Society of Clinical Oncology (ASCO) guidelines. In these guidelines, the following histopathological characteristics are considered unfavourable: perforation, T4, venous invasion, poorly differentiated or undifferentiated tumours, and fewer lymph nodes.

Considerations

Preferred Version of TNM Classification

There is no evidence to support the use of either TNM 1997 or TNM 2002 with regard to the definition of a lymph node. In practice, the 3-mm rule is easy to apply and reproducible, whereas the contour rule is in fact not reproducible. Use of the contour rule is only justified by its mention in the latest version of the TNM classification. The 3-mm rule is used in a number of other European countries (e.g., United Kingdom [UK], Belgium).

Prognostic Histopathological Factors in TNM Stage II Disease

There is a need to identify a subgroup of patients with TNM stage II disease that are suitable for adjuvant chemotherapy (see section "Adjuvant Chemotherapy" in the original guideline document) Selection is based on multiple factors, including poor differentiation (see appendix 12 in the original guideline document), perforation, pT4 disease, venous invasion, less than 10 lymph nodes evaluated,

and obstruction (clinical parameter). This selection process is not supported by evidence in the literature but is used in daily practice.

Assessment after Neoadjuvant Therapy

After neoadjuvant therapy, the degree of tumour regression should be determined. However, the most important factor is to assess the circumferential margin.

Considerations

The introduction of neoadjuvant therapy has changed the way in which resection specimens are assessed. This is of particular concern for cases of rectal cancer treated with long-term radiotherapy with or without chemotherapy. At this time, there is no indication that short-term neoadjuvant radiotherapy using 5x5 Gy in the week before surgery causes significant changes in histology. These specimens can be assessed according to the standard methods described in the section "Standard Pathology Report" above.

Several systems classify tumour regression into 1 of 5 categories. These systems have been combined by various authors using different methods to create 2-3 categories that correlate with prognosis. There is no consistent manner for determining tumour regression; moreover, the reproducibility of these systems is moderate at best. Unlike a positive circumferential margin, these systems have yet to demonstrate independent prognostic value.

It appears advisable to record whether or not there is evidence of regression, which may affect subsequent treatment decisions. Based on practical considerations, use of a three-tiered system is proposed (no regression, regression, or complete response).

Criteria for determining a complete response (no viable tumour present) have been agreed upon internationally due to the importance of standardisation. Initially, at least 5 sections are taken from the tumour region. If no viable tumour is found, then the entire tumour region is embedded. If again no viable tumour is found, then the blocks are sectioned at three levels. If again no viable tumour is found, then it is considered a complete response.

If mucinous lakes are found containing no viable tumour cells, it is considered negative for disease. The same applies for mucinous lakes present in lymph nodes. It appears reasonable to describe the latter separately, because the risk of developing distant metastases is increased in these patients. The lymph nodes themselves must be considered negative.

Immunohistochemistry (cytokeratins) has no role in the assessment of specimens following long-term neoadjuvant therapy. The assessment of traditional parameters, such as tumour type and differentiation grade, does not appear to be meaningful in this setting. Assessment of the circumferential margin is important: there is evidence that a positive margin has a greater predictive value after neoadjuvant therapy than when no neoadjuvant therapy is given. Tumour foci in

perirectal fat should be considered as discontinuous tumour invasion when determining tumour regression.

CRM and the Quality of Surgery

Assessment of the circumferential margin is standard for rectal cancer. A margin of 1 mm or less is considered positive. Margin status may be determined by the primary tumour or a lymph node.

The level of resection must be reported for the assessment of the resected specimen.

Considerations

Assessment of the circumferential margin is important for determining the prognosis of patients with rectal cancer. A margin of 1 mm or less is considered positive. If the margin is greater than 1 mm, it is advisable to include the exact margin in the report, because the risk of recurrence decreases as the margin increases.

There is evidence to suggest that a positive CRM negatively affects prognosis only when caused by the primary tumour. If a positive lymph node lies within the resection margin, the risk of local recurrence is not increased. Therefore, it seems prudent to base further actions on positive margins caused by primary tumour only (see section "Radiotherapy" below and in the original guideline document). The presence of any positive lymph node, however, should be reported.

According to the TNM classification, the circumferential or radial margin should be assessed using the R classification. This is not recommended. The R classification distinguishes between microscopically and macroscopically present tumour, independently of location (local, regional, or distant). In addition, the R classification begins with a margin of 0 mm, which can lead to confusion and underestimation of the number of positive margins.

The CRM should be determined after neoadjuvant therapy has been given.

Assessment of the quality of surgery based on total mesorectal excision (TME) specimens is a relatively new pathological parameter.

The results of the studies described above were confirmed in one unpublished study conducted in the UK involving 1,119 patients. From a practical standpoint and focusing on objectifying of the results, it is advisable to determine the level of resection, rather than the quality of surgery or completeness of the excision. The deepest resection level should be assessed. Photographic documentation is recommended.

The following resection levels are proposed:

- Level of resection at the muscularis propria (formerly incomplete)
- Level of resection at the mesorectal fat (formerly nearly complete)
- Level of resection at the mesorectal fascia (formerly complete)

If abdominoperineal resection is performed and the anal region is included in the resection, the region can be assessed as follows:

- Level of resection in the submucosa/perforation
- Level of resection in the sphincter region
- Level of resection beyond the sphincters

Treatment

Radiotherapy

All cases of rectal cancer should be discussed preoperatively in a multidisciplinary oncology review board.

When deciding whether to use radiotherapy, the advantages and disadvantages of treatment should be discussed thoroughly with the patient.

Preoperative radiotherapy using a biological effective dose (BED) $\geq$30 Gy is preferred over postoperative radiotherapy for patients with rectal cancer.

Radiotherapy is not indicated for patients likely to have T1N0 carcinoma based on preoperative diagnostic assessment.

Preoperative radiotherapy is indicated for all patients with T2-T4 disease, although a survival advantage has not been demonstrated. This applies to all patients regardless of the distance between the tumour and the anus.

For high-lying, relatively small tumours with no nodal involvement, radiotherapy can be omitted in exceptional cases; this must be agreed upon in a multidisciplinary oncology review board.

For cases in which a positive CRM is expected and for those cases in which four or more lymph nodes appear to be positive, combined chemoradiotherapy is preferred using a radiotherapy dose of 45-50 Gy (in fractions of 1.8-2 Gy). For all other patients, a short course of radiotherapy is recommended (5x5 Gy).

In principle, a conventional radiotherapy regimen should be combined with chemotherapy. A frequently used chemotherapy regimen is capecitabine 825 mg/m^2 bid, 7 days per week, for the duration of radiotherapy.

Considerations

<u>The Effects of Perioperative Radiotherapy on Local Control According to TNM Stage</u>

When analysing study results, it should be considered that the Dutch TME trial is the only study that evaluated standardised TME surgery. In this study, the absolute risk reduction per stage was markedly lower than that in the previously described meta-analyses: 0.2%, 4.7%, and 10.7% for stage I, II, and III disease, respectively. Similar absolute risk reductions of 3%, 6%, and 8% for stage I, II, and III, respectively, were found in the recently presented MRC-CR07 study,

which also used TME surgery and compared preoperative radiotherapy (5x5 Gy) with postoperative chemoradiation for patients with positive margins. Based on these results, it may be concluded that radiotherapy can be omitted for patients with stage I disease (T1-T2,N0). Given the difficulty in distinguishing diagnostically between T2 and T3 disease, it was decided to recommend omitting radiotherapy for T1N0 disease only.

For both preoperative and postoperative radiotherapy, improvements in local control are accompanied by an increase in adverse events. Several studies have shown that impairment of perineal wound healing increases and that defecation and sexual dysfunction can occur over the long term. In the Dutch TME study, the incidence of faecal incontinence increased from 40% in non-irradiated patients to 60% in patients undergoing radiotherapy. The incidence of sexual disorders increased from 56% to 68% in men and from 15% to 22% in women. When deciding whether to use radiotherapy, the advantages and disadvantages of treatment should be discussed thoroughly with the patient.

The Effect of Preoperative Radiotherapy on Survival According to TNM Stage

The reduction in cancer-specific mortality after preoperative radiotherapy is reflected in an improvement in overall survival in patients with stage II and III disease. However, based on the results in Table 2 in the original guideline document, it appears that radiotherapy correlates with an increase in death due to other causes. This may be due in part to the inferior radiotherapy techniques that were used in the past. With the more advanced techniques used today, this radiotherapy-related mortality is expected to decrease considerably. Countering the absolute risk reduction for local recurrence has decreased thanks to the introduction of TME surgery, which may make it more difficult to detect a survival advantage.

Are There Subgroups of Patients within Specific TNM Stages of Rectal Cancer that Derive More or Less Benefit from Radiotherapy?

Tumour Height

In the recently presented MRC-CR07 study, preoperative radiotherapy was associated with a reduction in local recurrence for all tumour heights. Preoperative radiotherapy reduced the rate of local recurrence from 10.0% to 6.0% for tumours 0-5 cm from the anus, from 10.0% to 5.0% for tumours 5.1-10 cm from the anus, and from 16.0% to 1.0% for tumour >10 cm from the anus. Notably, most of the tumours in the >10 cm group were located 10-12 cm from the anus. In a study conducted in Germany in which preoperative chemoradiation was compared with postoperative chemoradiation, patients with tumours > 10 cm from the anus had a similar local recurrence rate as those with tumours 5-10 cm from the anus. It is important to note that determining the distance between the tumour and the anal sphincter is extremely difficult. Based on these considerations, it does not seem advisable to omit radiotherapy for all tumours located more than 10 cm from the anus. For smaller tumours (T2, small T3) without lymph node involvement, omitting radiotherapy may be considered. Given the difficulty in determining tumour height, this should be decided in a multidisciplinary review board. Patient preference should also play an important role in this decision.

Positive Circumferential Resection Margin (CRM)

The recently presented MRC-CR07 study is the only randomised trial other than the TME study that used a standardised pathology approach to determining the CRM. In this study, patients with a positive CRM received postoperative chemoradiation if they had not received preoperative radiotherapy. The recurrence rate in CRM-positive patients was 16% for the preoperative group and 23% for the postoperative group.

A short course of preoperative radiotherapy therefore appears more effective than postoperative radiotherapy or chemoradiation in patients with positive CRM. However, the recurrence rate is high enough to warrant a radiotherapy regimen other than the 5x5 Gy schedule. Several studies have since demonstrated that the local recurrence rate is reduced in patients with a threatened CRM who receive neoadjuvant therapy and subsequently achieve a negative CRM during surgery. Although there are no data from randomised trials, it appears that conventional radiotherapy regimens (combined with chemotherapy) that induce downstaging are indicated for these patients.

When Is Chemoradiation (CRT) Indicated?

Assessment of trials of chemoradiation is hindered by the fact that various definitions of locally advanced disease were used. Most studies defined locally advanced disease as all T3 and T4 tumours and those with positive lymph nodes. Given that the TME trial demonstrated that a short course of preoperative radiotherapy provided adequate local control in stage III disease, it is recommended to limit the definition of locally advanced disease to all T4 tumours and T3 tumours with a threatened CRM on preoperative MRI. A patient should also be considered to have locally advanced disease if preoperative diagnostic evaluation indicates the presence of four or more positive lymph nodes (cN2 disease).

The combination of 5-fluorouracil (5-FU) and leucovorin (LV) is the chemotherapy regimen used in all recent, randomised studies of locally advanced rectal cancer. Several phase I and II studies, however, have used capecitabine (an oral 5-FU analogue) as a radiosensitiser. All of these studies used a radiotherapy dose of at least 50.4 Gy and various doses and schedules of capecitabine. The toxicity profile found in these studies was acceptable and did not appear to be worse than that of intravenous 5-FU. Given the practical advantages of capecitabine (at-home use rather than hospital admission), it is recommended to use capecitabineÂ 825 mg/m^2 bid for chemoradiation.

Some reports have described the use of intraoperative radiotherapy (or brachytherapy) for cases of primarily unresectable disease treated with chemoradiation for which radical resection is then deemed unfeasible. A number of these non-randomised studies have achieved promising results with this technique. For patients who have undergone chemoradiation and for whom it is then determined preoperatively that radical resection is not possible, intraoperative radiotherapy or brachytherapy may provide additional value with regard to local control.

Surgery

Site of Local Excision

Local excision is a good alternative for patients diagnosed preoperatively with T1 rectal cancer based on biopsy and endorectal ultrasound.

If local excision of rectal cancer is considered, then total mesorectal excision (TEM) is the preferred method. For relatively small and distally located rectal cancer, transanal excision (TAE) may be considered.

Local excision alone is sufficient for moderate or well differentiated stage T1 rectal cancer with no evidence of lymphangio- or vasoinvasive growth (T1 G1/2L0/V0) that is excised with tumour-free margins.

Thorough pathologic assessment is required to determine tumour-free margins after local resection.

If after TEM it appears that the disease stage is more involved than T1G1/2L0/V0, then an additional TME should be performed, preceded by radiotherapy (5x5 Gy).

Re-excision can be considered if local resection does not yield tumour-free margins, but only in cases of T1G1/2L0V0 rectal cancer.

Follow-up after local excision should include rectoscopy with endorectal ultrasound every 3 months for the first 2 years, in addition to standard follow-up for TME.

Local excision of rectal cancer with curative intent should only be performed in a hospital with adequate facilities and expertise (e.g., TEM, rectoscopy, endorectal ultrasound, standardised pathologic evaluation).

<u>Considerations</u>

The available literature on local excision of rectal cancer is limited in scope and detail. However, it can be determined that all local techniques are safer than TME with regard to morbidity and mortality. Compared with TAE, TEM is better able to excise larger and more proximally situated tumours. Positive surgical margins are a significant prognostic factor for the development of local recurrence after local resection.

Positive surgical margins are found more frequently after TAE than after TEM. Therefore, TEM appears to be a better technique than TAE for excising rectal tumours. Moreover, with TEM, it may be less likely that a subsequent TME will be necessary for technical or pathological reasons.

For patients with stage T1 disease, use of TEM must be limited to those with well or moderately differentiated tumours without lymphangio- or vaso-invasive growth (G1/2,L0,V0). This produces rates of local recurrence and survival that are comparable to those achieved with TME. For T1 disease without these low-risk factors, the evidence is too limited to draw conclusions regarding the efficacy of TEM. Local excision is not recommended for the treatment of stage T2 disease or higher based on the inferior efficacy results compared with TME.

Unfortunately, it is not often possible to determine the risk profile based on biopsies obtained preoperatively. The absence of low-risk factors (T1G1/2L0V0) in the TEM-resected specimen should prompt a secondary TME. In this scenario, TEM resection could be considered a large biopsy.

Consequently, TME should be preceded by radiotherapy (5x5 Gy). One biopsy is insufficient to confirm T1 disease preoperatively, and endorectal ultrasound is recommended (see section on "Diagnosis" above and in the original guideline document). This is preferably combined with rigid rectoscopy to obtain adequate anatomical localisation of the tumour.

No conclusions can be drawn from the available literature regarding the optimal frequency and method of follow-up. Anecdotal reports suggest that intensive follow-up with rectoscopy and endorectal ultrasound allows for surgical treatment of local recurrence. Only TEM is insufficient for stages higher than low-risk T1 disease. Published data on the combination of local excision and adjuvant or neoadjuvant therapy are too limited to make guideline recommendations.

Total Mesorectal Excision (TME)

It is recommended to perform radical surgery for rectal cancer according to the TME principles.

For tumours located distally, a low anterior resection can be considered provided that a distal margin of 1-2 cm is feasible. For tumours situated proximally, resection of the distal mesorectum can be omitted provided that a distal margin of 5 cm can be maintained.

It is recommended to base the use of abdominoperineal resection (APR) or low anterior resection (LAR) for the treatment of rectal cancer on the preoperative assessment of tumour height, T stage (for distal tumours), comorbidity, patient age, preoperative sphincter function, and patient preference.

<u>Considerations</u>

Efficacy of Total Mesorectal Excision vs Conventional Excision

Anastomotic leakage has been reported more frequently since the introduction of TME, but two studies have noted that the incidence decreased as the experience level of surgeons increased.

Influence of Distal Margin on Rates of Local Recurrence and Survival

The working group is of the opinion that a distal margin of 1-2 cm is sufficient for total mesorectal excision in which the entire mesorectum is resected up to the point just above the sphincter. For tumours located in the proximal rectum, i.e., above the peritoneal reflection, it is not necessary to resect the entire mesorectum. In this case, a distal margin of 5 cm can be considered sufficient. This however, does not preclude following the principles of TME as described in the 'Literature review' (see original guideline document). Radical resection with a

circumferential margin of at least 1 mm remains the foundation of surgical management of rectal cancer.

Difference in Effects of LAR and APR on Quality of Life in Patients with Rectal Cancer

In the literature, it appears that patients with lower rectal cancer undergoing abdominoperineal resection have a poor prognosis. This was observed in multiple studies, including the Dutch TME study. Treatment of lower rectal cancer (0-5 cm from the anus) with abdominoperineal resection is associated with a high rate of positive circumferential margins, local recurrence, and shorter survival. The perineal resection was performed up to the sphincter in 64% of cases and into the sphincter or to the mucosa in the remaining 36% of cases. It is likely that the higher rate of positive circumferential margins and poorer outcomes seen with low-lying rectal cancer is due to the anatomy of the distal rectum. The mesorectal fat layer thins out here, which means that resection in the TME plane inherently extends up to the rectal musculature. In recent years, abdominoperineal resection without opening the distal mesorectal plane has been promoted. Perineal resection is then performed more radical, resecting the levator ani muscle near the point of its insertion into the obturator muscle. This provides a specimen with wider margins around the tumour. This technique is referred to as a cylinder TME, because the specimen lacks the traditional cinching at the site of the sphincter.

Laparoscopic Surgery

Laparoscopic surgery for **colon cancer** is safe and at least as effective as open surgery, provided that the surgeon has sufficient expertise.

Given the lack of sufficient evidence regarding the relative efficacy of laparoscopic surgery and open surgery for **rectal cancer**, laparoscopic surgery for rectal cancer should only be performed in a controlled setting (e.g., trial, audit) and in the presence of sufficient expertise.

Given the prolonged learning curve associated with laparoscopic surgery, it is very important that the surgeon is adequately trained before practicing this technique on his or her own.

The American Society of Colon and Rectal Surgeons (ASCRS) and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) have developed minimum requirements that surgeons must meet before they can perform laparoscopic surgery with curative intent in patients with cancer.

Surgeons must perform at least 20 laparoscopic colon operations for benign or incurable diseases before starting laparoscopic colon surgery with curative intent. The working group is of the opinion that these international guidelines should also be applied in the Netherlands. It should be noted that the first 20 procedures are performed preferably under the supervision of an expert surgeon. Under these conditions, both benign and curative laparoscopic colorectal resections can be performed.

<u>Considerations</u>

Shorter Duration of Hospitalisation

In regard to the shorter duration of hospitalisation with laparoscopic colorectal surgery, it should be noted that this has not been compared with the similarly shorter duration of hospitalisation achieved with enhanced recovery programmes. Randomised prospective trials evaluating the relative contribution of multiple factors are ongoing (e.g., the LAFA trial).

Cost-Effectiveness

See the "Cost Analysis" field.

Learning Curve and Implementation

The laparoscopic technique for colorectal resection is a difficult technique. Surgeons who wish to use this technique follow a clear learning curve that has been described in the literature as comprising procedures. One study author calculated that the learning curve for an individual surgeon required at least 50 procedures for the laparoscopic treatment of colon cancer. This number is likely to be higher for the laparoscopic treatment of rectal cancer. The prolonged learning curve hinders rapid adoption of the technique and safe implementation. Establishment of a good programme to train surgeons who wish to use this technique is warranted. Rapid introduction of the laparoscopic technique without an established training programme will lead to poor laparoscopic results. Good patient selection is also important to compensate for the relative lack of expertise.

Colon Cancer vs. Rectal Cancer

The studies identified in the recent Cochrane review on rectal carcinoma were of moderate quality. For this reason, the working group adopted a conservative approach when formulating recommendations on the use of laparoscopy in patients with rectal cancer.

Centralisation of T4 and Locally Recurrent Disease

Stage T4 and locally recurrent rectal cancer should be treated in a specialised centre with sufficient relevant expertise.

Some neoadjuvant therapy may be given at a regional centre in close consultation with the specialized centre.

To gain further insights on treatment techniques, a transparent registry should be established and general treatment outcomes should be reported on a regular basis.

Support for the function of the specialised centre will require the realisation of adequate data registration and reporting.

<u>Considerations</u>

Expertise in recognising recurrent/advanced rectal cancer must be present in all hospitals treating rectal cancer. Local staging requires sufficient MRI capabilities using high resolution with T2-weighted images in multiple planes. Abdominal/thoracic CT can be used for distant metastases.

The resectability of cases of obvious T4 or locally recurrent disease must be discussed in a specialised centre before neoadjuvant therapy (if necessary) begins. Not all cases of advanced rectal cancer have to be treated in a specialised centre. Grey areas include the management of patients with tumours that threaten the circumferential margin but are far away enough that a TME-like procedure can be performed after long-term neoadjuvant therapy. These patients are eligible for neoadjuvant radiotherapy or chemotherapy, and the response can be assessed first in the regional hospital with MRI and clinical evaluation. If the tumour has in fact regressed and the margins have become adequate, TME can be performed.

If, however, these patient continue to have considerable fibrosis up to the threatening margin, or if the tumour remains fixed (if located distally and within reach of digital rectal examination), referral to a specialised centre should be considered.

Chemoradiation plays an important role in the management of T4 locally advanced disease and locally recurrent disease. Most centres that provide radiotherapy will be familiar with long-term neoadjuvant chemoradiation regimens, because this approach is also indicated for cases of less advanced rectal cancer. These regimens are also applied in the palliative setting. Experience with re-irradiation for locally recurrent disease is less common, but some institutions have already gained considerable experience with this approach, whereby centralisation of re-irradiation did not appear necessary. It may be concluded that diagnosis and neoadjuvant treatment of patients with local recurrence or T4 disease can be performed in the referring hospital or, in any case, within the referring region. Certain diagnostic tests, such as positron emission tomography/computed tomography (PET/CT) with standard uptake value (SUV) to determine the response to neoadjuvant therapy, may be better performed centrally.

Furthermore, it is important the most patients are treated within the context of a clinical trial to gain further insights into this relatively small group of patients. It is therefore preferable that patients are seen at the beginning of the treatment trajectory at both the referring hospital and a specialised centre, even for centralised, temporary treatment.

Adjuvant Chemotherapy

The working group is of the opinion that, based on the conclusions described in the original guideline document, no clear recommendations can be made regarding the use of adjuvant chemotherapy. Preferably, patients should be treated in clinical trials.

Considerations

The studies and meta-analyses described in the original guideline document are based primarily on chemotherapy regimens that are not available or no longer used. Studies conducted in the United States of America (USA) often used semustine, which failed to improve results when added to 5-FU but did increase the risk of developing leukaemia. Studies conducted in Japan often used oral preparations of 5-FU and/or mitomycin. However, all of the studies used 5-FU-based regimens. It therefore seems reasonable to assume that 5-FU is partly or fully responsible for the observed effects.

Adjuvant chemotherapy for rectal cancer as reported in most of the aforementioned studies continues to be given after surgery with or without postoperative radiotherapy. Local therapy has since changed: TME has become the standard and is frequently preceded by a short course of radiotherapy (5x5 Gy) or long-term radiotherapy or chemoradiation. The effects of adjuvant chemotherapy following TME have been evaluated in only one adequate trial. In this study, however, patients underwent lateral lymphadenectomy, which is not performed in the Netherlands. This study found a positive effect on survival.

The question remains whether the effects of chemotherapy are expected to be different in the setting of TME than what has been observed with outmoded types of surgery. The risk of haematogenous micrometastases at the time rectal cancer is diagnosed, i.e., before local treatment has begun, naturally remains unchanged. The risk of local recurrence and later haematogenous metastases does decrease dramatically with neoadjuvant radiotherapy and TME. However, this is not relevant to predicting the efficacy of adjuvant chemotherapy at the time of diagnosis.

Is it reasonable to assume that the effects of adjuvant chemotherapy are different in colon cancer and rectal cancer? In the metastatic setting, no distinction is made between colon and rectal cancer with regard to systemic therapy. It seems illogical to think that the effects of adjuvant chemotherapy on tumours of the large intestine would depend on their approximate distance from the anus.

It should be noted that adjuvant chemotherapy is recommended or mentioned as a standard in guidelines from other countries, including Canada, the USA, Australia, UK, and France, based on the data described above. Regarding the choice of chemotherapy regimen, all studies published to date have used 5-FU or 5-FU analogues alone or in combination with leucovorin or levamisole.

Results from phase III trials evaluating the combination of 5-FU or 5-FU analogues with newer agents, such as oxaliplatin, irinotecan, and bevacizumab, are not yet available. An Intergroup study conducted in the USA uses FOLFOX (5-fluorouracil, leucovorin, oxaliplatin) as standard adjuvant therapy and is evaluating the addition of bevacizumab in patients with stage II and III rectal cancer.

Follow-up

Routine Follow-up

General

The person responsible for coordinating follow-up must be clearly defined per hospital and per patient.

T1N0

- Check-ups every 6 months for the first 2 years after surgery, then annually for up to 5 years after surgery, followed by colonoscopy every 6 years.
- Physical examination only as indicated; for rectal carcinoma, digital rectal examination every 6 months.
- Routine carcinoembryonic antigen (CEA) assessment and diagnostic imaging are not indicated due to their low diagnostic yield.

All Other Tumours without Distant Metastases

- Colonoscopy within the first 3 months after surgery if complete colonoscopy was not possible before surgery.
- Check-ups every 6 months for the first 2 to 3 years after surgery, then annually for up to 5 years after surgery. For rectal cancer, also include digital rectal examination every 6 months.
- Hepatic ultrasound every 6 months for the first year after surgery, then annually for up to 5 years after surgery. CT scan is indicated if ultrasound cannot be performed easily for technical reasons, e.g., patients with obesity or air in the intestines.
- CEA assessment every 3 to 6 months for the first 3 years after treatment, then every 6 months for up to 5 years after treatment.
- Colonoscopy 2 to 3 years after surgery, according to the consensus on follow-up of colon polyps (6 years for 0-2 polyps, 3 years for 3 or more polyps). If complete colonoscopy is not possible, CT colonography is an alternative.

Stage IV

Individual follow-up policy, depending primarily on the type of therapy (chemotherapy or no chemotherapy).

Considerations

The early detection of metastases is more important today than ever before, due in part to the advent of improved treatment options (liver surgery, radiofrequency ablation [RFA], chemotherapy).

In addition to early detection of metastases, recurrence, and metachronous tumours, there are other reasons to monitor patients with colorectal carcinoma. The most important additional reason is to provide the patient with information about the disease. Patients often have many questions about the disease, particularly in the period immediately following treatment.

The operations that are performed are often invasive, as are the consequences, such as for patients with a stoma. In addition, there may be some uncertainty about the prognosis. Other arguments supporting follow-up are the opportunity for the treating clinicians to check the outcomes of their intervention, the cancer registry, and participation in clinical trials or training. Above all, most patients

value routine check-ups, even though some tests, such as colonoscopy, can be a burden.

Arguments against routine check-ups include medicalisation, constantly returning stress, unnecessary follow-up tests due to false-positive results (which incidentally have little impact if follow-up is limited to CEA assessment and hepatic imaging), and higher costs. In light of these disadvantages, a case can easily be made for less intensive or no follow-up, particularly in patients with T1N0 colorectal cancer. Therefore, a stratified approach to follow-up has been selected.

In recent years, new and better chemotherapeutic options (second- and third-line therapies) have become available for patients with advanced or metastatic colorectal cancer, which justifies considering starting treatment early, i.e., before symptoms occur. It has also been demonstrated that the results of chemotherapy are better if the Karnofsky index of the patient is better. Thus it appears reasonable to assume that initiating chemotherapy relatively early in patients in acceptable condition is better than waiting until extensive metastases are present.

New imaging techniques (CT colonography and specialised endoscopy), genomics and proteomics in faecal samples, and specific histological/immunohistochemical techniques in tumour specimens appear promising, but are too early in development to be included in the current approach to follow-up.

In formulating the recommendations, the working group has taken into account current practices and the recommendations found in other guidelines (see appendix 7 in the original guideline document).

Different follow-up schedules have been devised for Hereditary colorectal cancer (in Dutch) and patients undergoing TEM.

Metastases: Treatment

For asymptomatic patients with measurable, unresectable metastases, systemic therapy should not be delayed for a long period.

The combination of fluoropyrimidine-containing chemotherapy plus bevacizumab is considered standard first-line treatment for patients in relatively good condition (World Health Organization [WHO] performance status 0-1) without risk factors related to bevacizumab use.

Treatment with oral fluoropyrimidines is preferred over 5-FU/LV because they are associated with less frequent adverse events and can be given safely in combination with other agents.

There is no preference between the use of oxaliplatin or irinotecan as a component of first-line combination chemotherapy. If irinotecan is combined with 5-FU, the 5-FU should be given as a continuous infusion and not as a bolus infusion, because the latter method is associated with more severe adverse events.

First-line combination chemotherapy with a fluoropyrimidine and irinotecan or oxaliplatin provides no significant benefit in overall survival, compared with the sequential administration of these agents.

Treatment with hyperthermic intraoperative peritoneal chemotherapy (HIPEC) may be considered for patients with metastases limited to the abdominal cavity, provided that the number of metastatic sites is limited and the metastases can be removed radically by surgery.

Considerations

Data from well-designed prospective trials that provide insight into the optimal time to start systemic treatment are lacking. Given the increasingly better survival results in conjunction with the availability of multiple therapeutic options, it does not appear reasonable to delay treatment in asymptomatic patients until symptoms occur.

At this time, there is insufficient evidence from randomised controlled trials on the use of oral fluoropyrimidines vs 5-FU in combination with irinotecan or oxaliplatin. Based on results from phase II trials and preliminary results from phase III trials, it appears that the efficacy and toxicity of capecitabine plus oxaliplatin and capecitabine plus irinotecan are similar to that observed with FOLFOX and FOLFIRI (5-FU, leucovorin, irinotecan), respectively.

There is no clear benefit to combination chemotherapy, compared with sequential therapy. Given the availability of multiple effective agents and the poor prognosis of the vast majority of patients, preference could be given to first-line combination chemotherapy. On the other hand, first-line monotherapy with a fluoropyrimidine is a less toxic treatment approach that provides a similar survival benefit, provided that it is followed by appropriate subsequent therapy. A first-line single-agent chemotherapy regimen may be easier to combine with 'targeted' therapies.

Communication

In accordance with the Wet op de geneeskundige treatments overeenkomst (WGBO), the working group wishes to emphasise that a patient with colorectal cancer should be thoroughly informed about his/her disease and the advantages and disadvantages associated with the available treatment options.

Within a hospital, it should be clearly defined which care provider in which setting is responsible for informing the patient.

It should be made clear to the patient who the coordinating care provider is.

The patient should be informed about the existence of relevant patient organisations: De Nederlandse Stomavereniging and Stichting Doorgang.

Considerations

In order to make sound decisions, it is important that all relevant parties clearly understand which phase the disease process is in (the 'consciousness context'). Treatment goals change over time from cure through palliation aimed at maintenance of quality of life while minimising the disease burden to, ultimately, symptom control in the palliative terminal phase.

The proportionality of treatment is an important consideration, whereby the patient's capacity and preferences play a large role. Patient preferences are determined by physical, psychological, social, and philosophical factors. Awareness of these factors by the treating physician is important to arrive at a balanced decision, particularly in the event of disease progression. A multidisciplinary approach may be necessary to achieve sound decisions and the necessary related emotional support.

Another important aspect in the decision-making process is anticipatory management and communication. Based on the diagnosis, disease course, comorbidity, and prognosis, the physician should estimate the expected symptomatology. Anticipating these symptoms enhances the patient's trust in the treatment plan and improves quality of life.

Determining which care provider is the best candidate for informing the patient depends on the phase of the disease and hospital-related factors. The easiest approach is to assign the responsibility to the care provider considered the treating physician for that specific phase of the disease (for colorectal carcinoma, this may be the gastroenterologist, surgeon, or medical oncologist). The oncology nurse may also play a role, under the supervision of the treating physician. Preferably, clear agreements are made within a hospital with regard to which care provider is responsible for informing the patient at different points in the treatment process.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The classification of support and level of evidence are reported in each chapter of the original guideline document. The most important articles upon which the conclusions are based are mentioned in the 'Conclusions' section. A description and assessment of the articles can be found in the different sections under the tab 'Literature review'. The scientific evidence is summarised in the 'Conclusions' section, in which the level of the most relevant evidence is reported.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Better treatment and thereby better outcomes for patients with rectal cancer

POTENTIAL HARMS

- Adverse events associated with radiotherapy: impairment of perineal wound healing, defecation dysfunction, sexual dysfunction, mortality
- Prolonged learning curve associated with performing laparoscopic surgery
- Disadvantages of laparoscopy: longer duration of surgery, higher costs
- Surgical complications and side effects: blood loss, anastomotic leakage
- Postoperative pain
- Side effects and complications of chemotherapy

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Guidelines are not legal requirements, but rather scientifically founded and widely accepted views and recommendations to which healthcare providers would have to adhere to provide quality care. Given that guidelines are based on 'average patients', healthcare providers can deviate from the recommendations in the guideline as necessary in individual cases. Deviation from the guideline is in fact sometimes necessary if the patient's situation demands it. When there is deviation from the guideline, however, it must be rationalised, documented and, when necessary, discussed with the patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and Evaluation

During the different phases of development of the draft guideline, consideration was given whenever possible to the implementation of the guideline and the actual feasibility of the recommendations. The guideline was distributed to all hospitals and oncology boards, scientific societies, and Comprehensive Cancer Centres (Integrale Kanker Centra). A summary of the guideline was also published in the *Dutch Journal of Medicine (Nederlands Tijdschrift voor Geneeskunde)*, and attention will be given to the guideline in various specialty journals. In addition, the guideline will be made available on www.oncoline.nl, and key text will be reproduced on the website of the CBO (Dutch Institute for Healthcare Improvement). To stimulate the implementation and evaluation of this guideline, the working group will, as a next step, create a list of indicators through which implementation can be measured. Indicators give healthcare providers the opportunity to assess whether they are providing the desired level of care. They can also be used to identify topics for improving the provision of care. The guideline will be tested by end-users in different regions and scientific societies, at which time on-site visits will also be organised.

IMPLEMENTATION TOOLS

Foreign Language Translations
Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

End of Life Care
Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Working Group on Gastrointestinal Cancers. Rectal cancer. Amsterdam, The Netherlands: Association of Comprehensive Cancer Centres (ACCC); 2008 Oct 14. 82 p. [306 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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Association of Comprehensive Cancer Centres - Disease Specific Society

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GUIDELINE COMMITTEE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in English and Dutch in Portable Document Format (PDF) from the Association of Comprehensive Cancer Centres Web site.

Print copies: Available from the Association of Comprehensive Cancer Centres PO Box 19001, 3501 DA Utrecht, The Netherlands

AVAILABILITY OF COMPANION DOCUMENTS

A version of the guideline for Personal Digital Assistants (PDAs) is also available at the Association of Comprehensive Cancer Centres Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on July 10, 2009. This information was verified by the guideline developer on October 20, 2009.

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